

Normal cellular response to chemoattractant signaling.

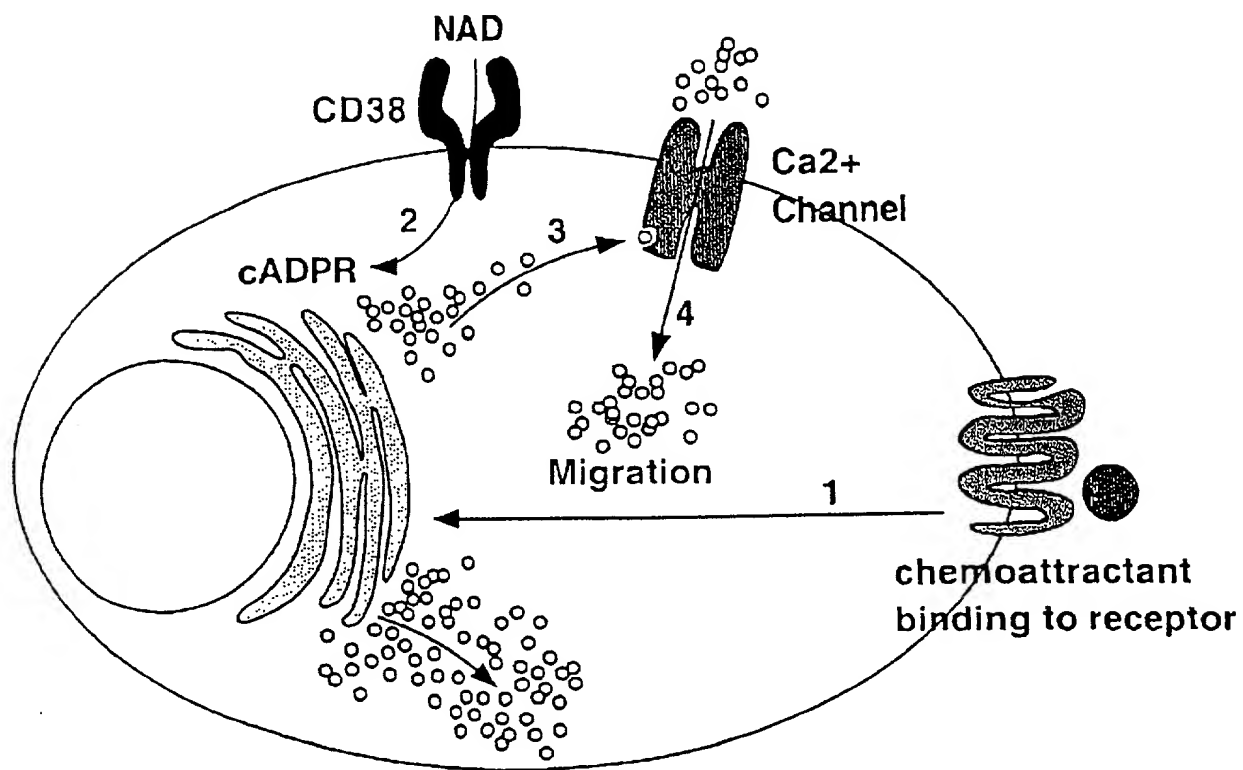


Figure 1

Inhibitors of cADPR production  
by CD38 prevent capacitative  
Ca<sup>2+</sup> entry and chemoattractant  
induced migration

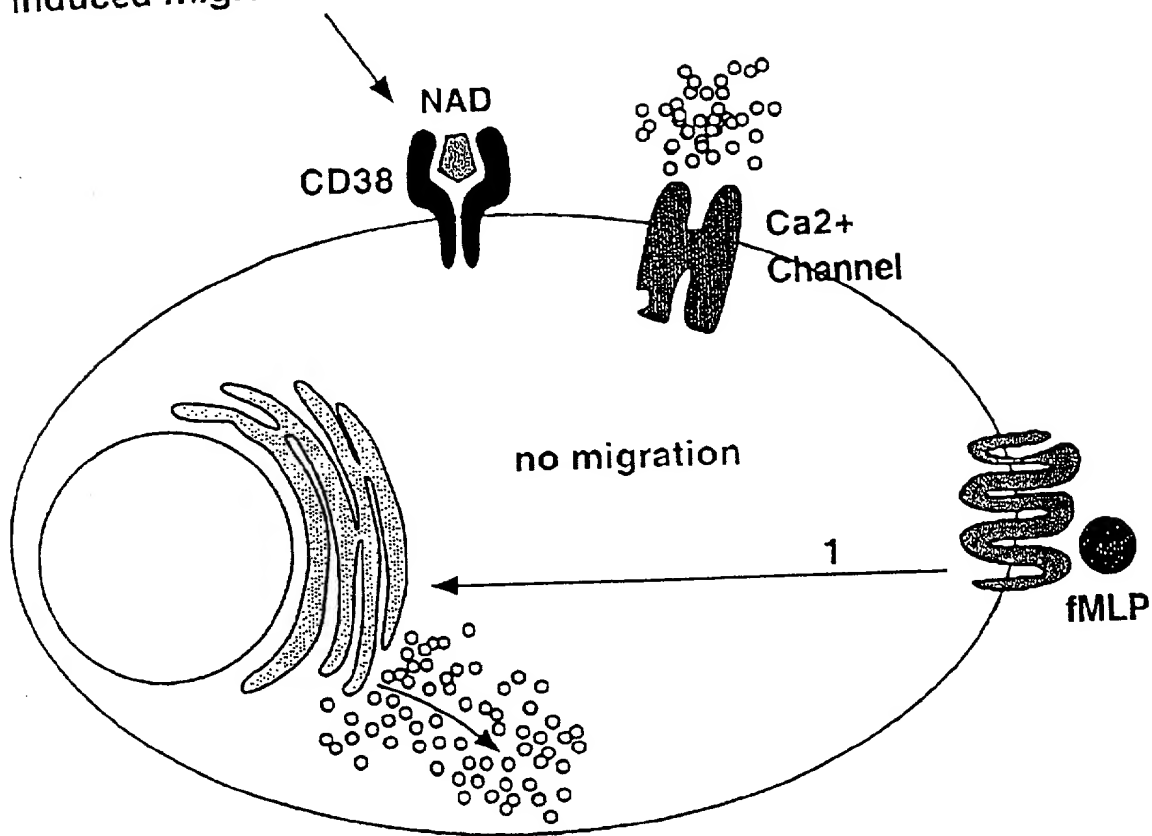


Figure 2

Proteins that regulate CD38 enzyme activity (screens will identify compounds that activate or inactivate these proteins)

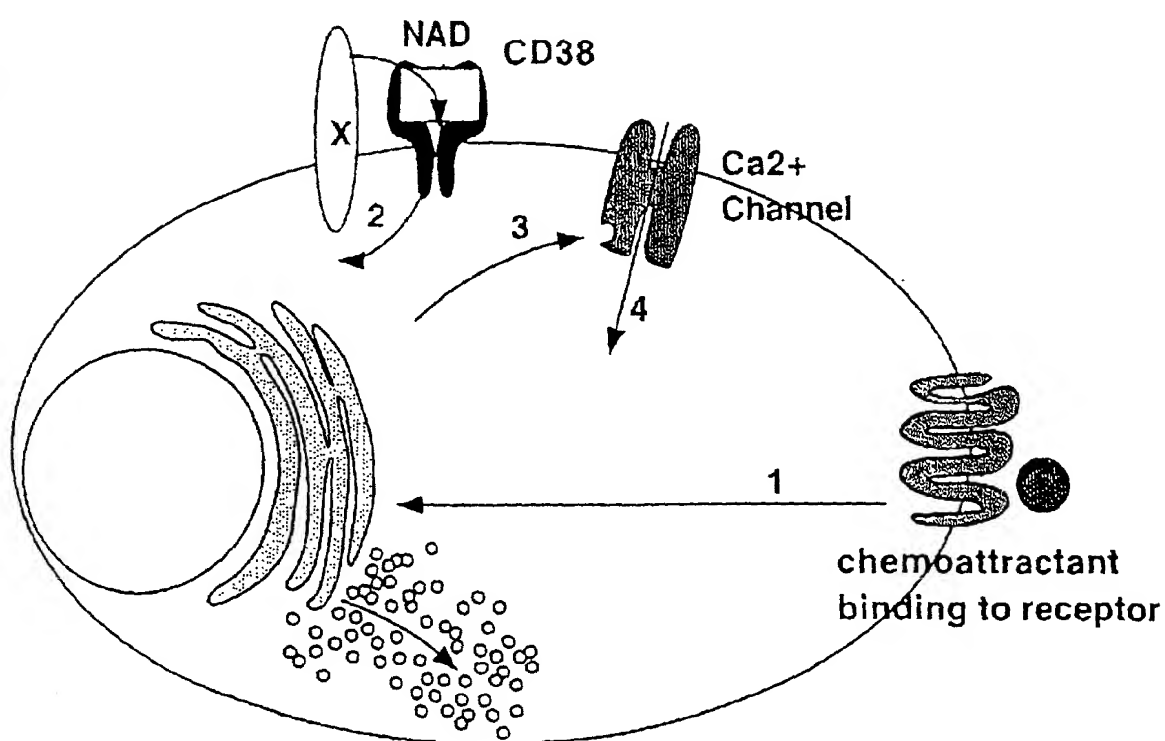


Figure 3

Proteins that regulate CD38 expression (screens will identify compounds that activate or inactivate these proteins)

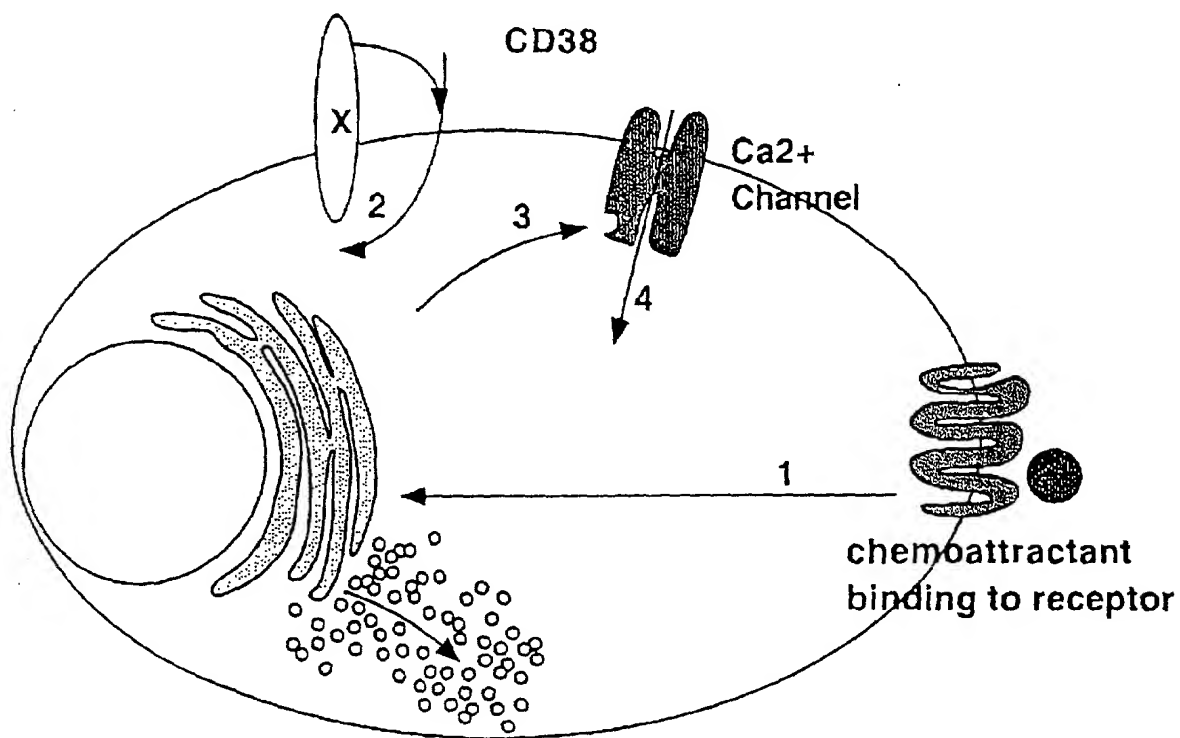


Figure 4

Alternative substrates for CD38 may  
generate inhibitors of cADPR and  
prevent capacitative  $\text{Ca}^{2+}$  release

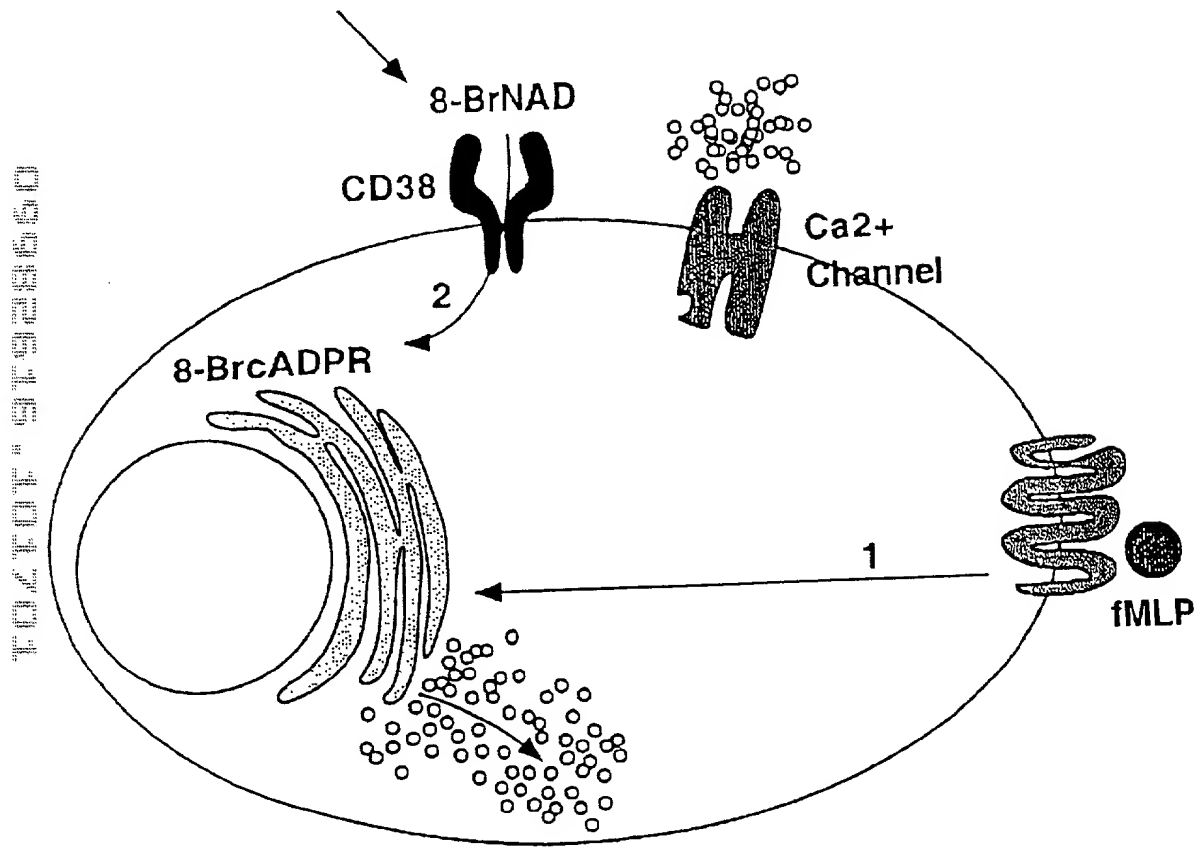


Figure 5

Inhibitors of cADPR binding  
block capacitative  $\text{Ca}^{2+}$  influx

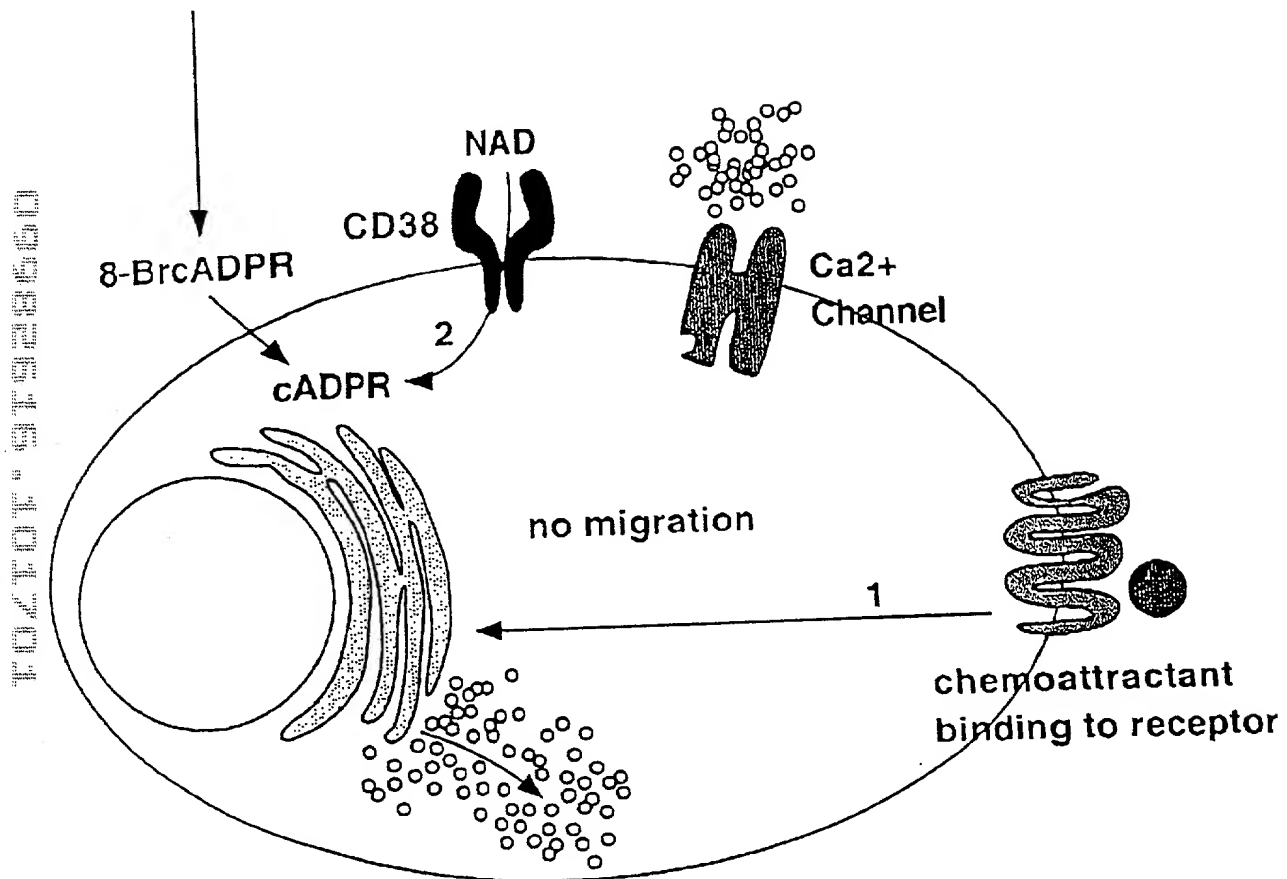
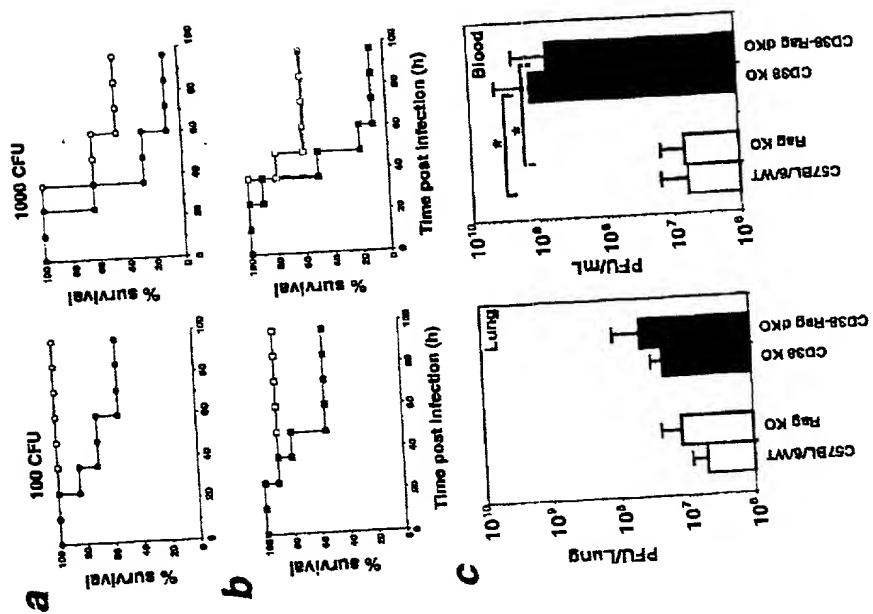


Figure 6

Figure 7 A-C



10/16/01 13:04 FAX 518 891 5126

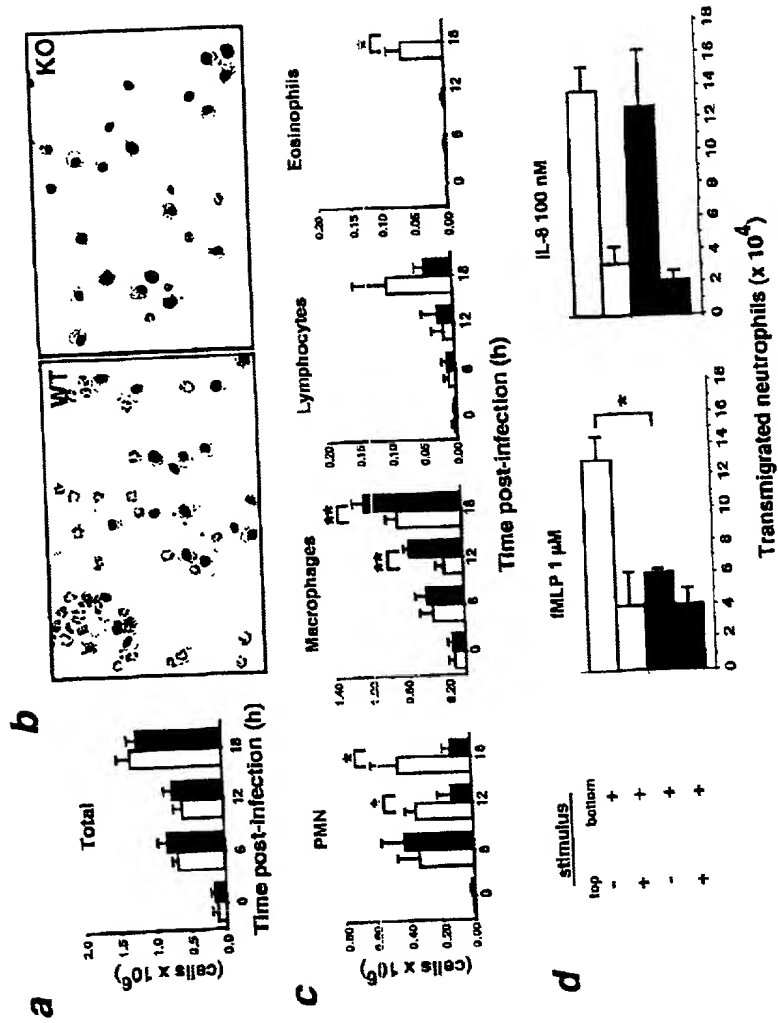
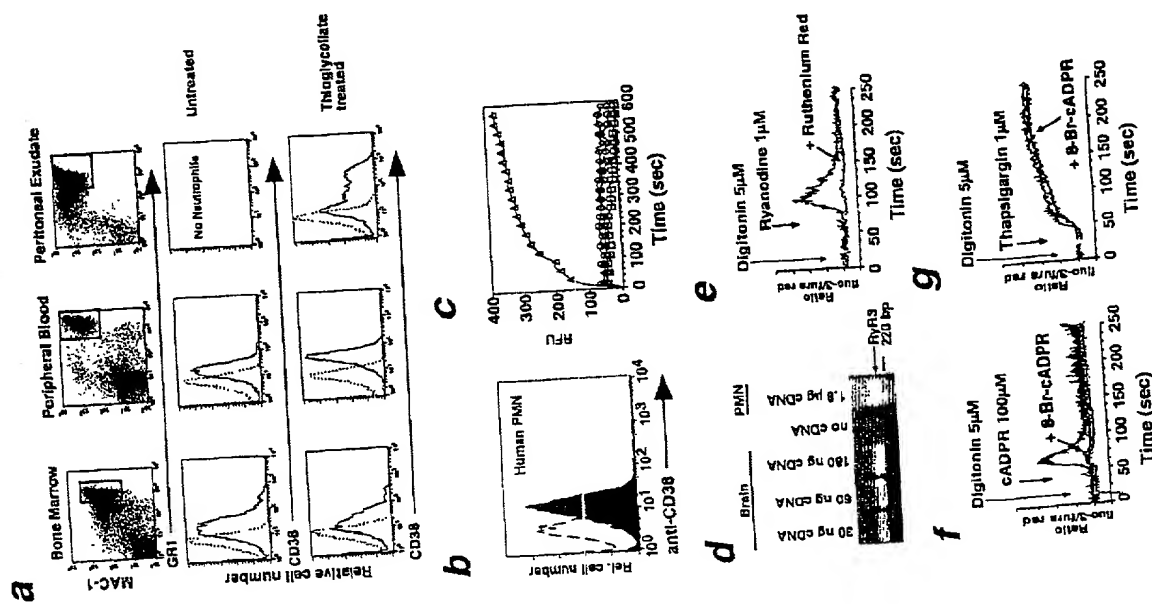
[illegible]

Figure 8 A-D



Figure 9A-G



0992615 101701

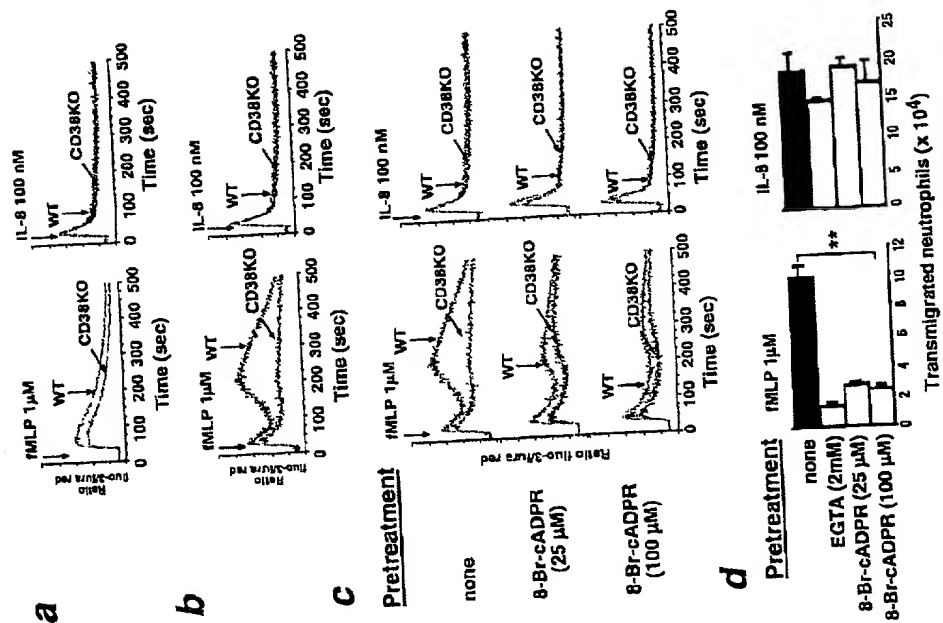


Figure 10 A-D

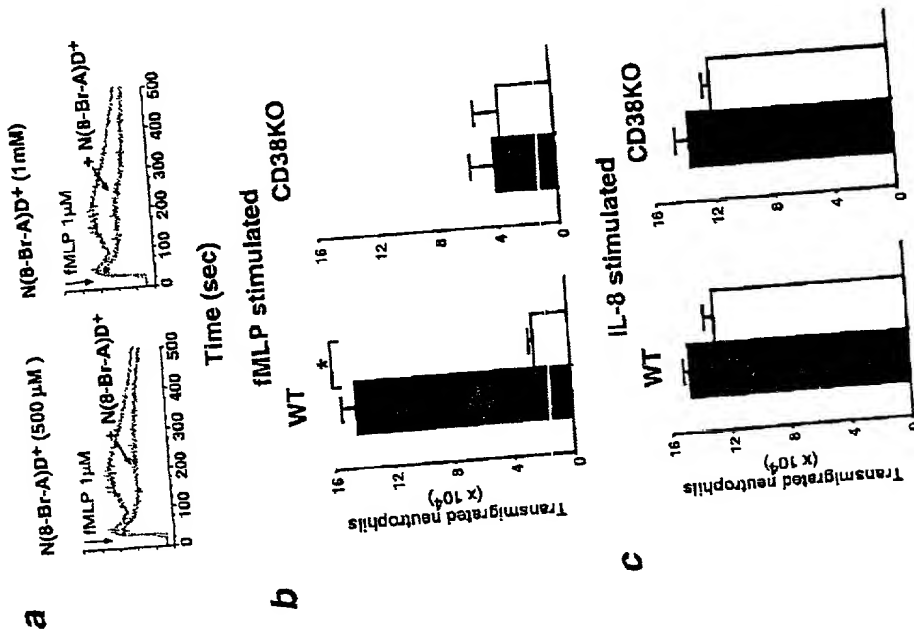


Figure 11A

FOR STAGE

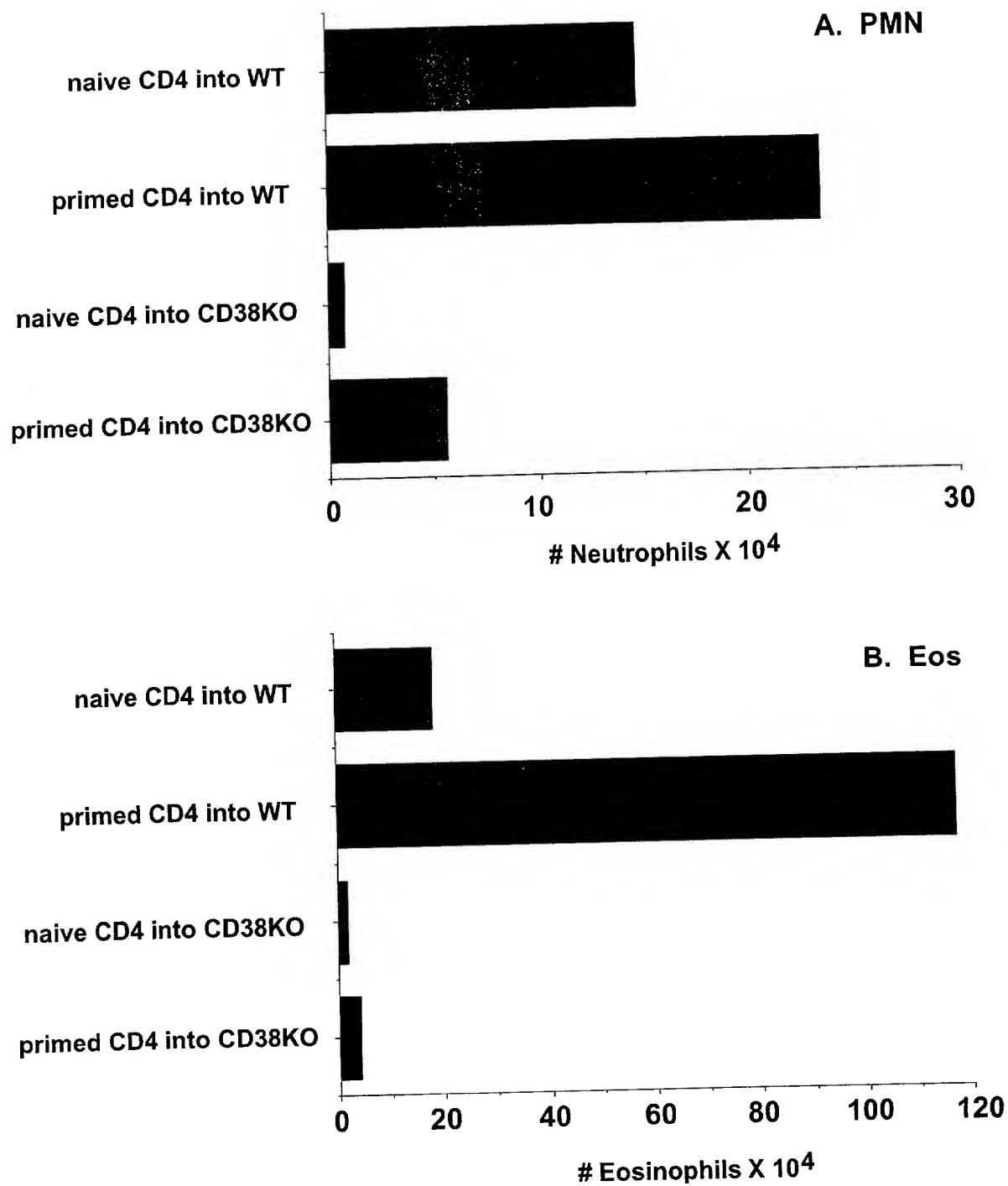


Figure 12

Consensus	GGAAAGAACG TAGACATATA TTGTTATATA GATTGTTC A GTTATTTTC	50
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	-----	
SM38	GGAAAGAACG TAGACATATA TTGTTATATA GATTGTTC A GTTATTTTC	50
Consensus	ACAATCTTTT AATTCAAATA ATGATGAACG TAATATTGTT TCTTACTTTA	100
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	-----	
SM38	ACAATCTTTT AATTCAAATA ATGATGAACG TAATATTGTT TCTTACTTTA	100
Consensus	TCAAATATTT TTGTCITTTAA CTCTGCACAA CATCAAATAA ACTTACTTAG	150
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	-----	
SM38	TCAAATATTT TTGTCITTTAA CTCTGCACAA CATCAAATAA ACTTACTTAG	150
Consensus	TGAAATAGTA CAATCACGAT GTA CTCTCAGTG GAAGGTTGAA CATGGAGCTA	200
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	-----	
SM38	TGAAATAGTA CAATCACGAT GTA CTCTCAGTG GAAGGTTGAA CATGGAGCTA	200
Consensus	CTAATATAAG TTGTAGTGAG ATCTGGAATT CATTTGAAAG CATTTTACTT	250
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	-----	
SM38	CTAATATAAG TTGTAGTGAG ATCTGGAATT CATTTGAAAG CATTTTACTT	250
Consensus	TCAACTCATA CTAATCAGC ATGTGTTATG AAATCAGGGT TATTCGATGA	300
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	-----	
SM38	TCAACTCATA CTAATCAGC ATGTGTTATG AAATCAGGGT TATTCGATGA	300
Consensus	TTTTGTTTAT CAATTGTTTG AATTGGAACA ACAACAACAA CAGCGACACC	350
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	-----	
SM38	TTTTGTTTAT CAATTGTTTG AATTGGAACA ACAACAACAA CAGCGACACC	350
Consensus	ACACAATTCA AACGGAACAA TACTTCCATT CTCAAGTGAT GAACATCATT	400
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	-----	
SM38	ACACAATTCA AACGGAACAA TACTTCCATT CTCAAGTGAT GAACATCATT	400
Consensus	CGTGGAAATGT GTAAACGTCT TGGAGTATGT CGTTCTCTAG AAACATACATT	450
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	-----	
SM38	CGTGGAAATGT GTAAACGTCT TGGAGTATGT CGTTCTCTAG AAACATACATT	450

[illegible]

Consensus	TCCAGGATAT CTGTTTGATG AATTGAATTG GTGTAATGGC AGTTTAAACAG	500
EST AWO17229 comp	-----	
EST A1067047 comp	-----	
EST N20756	TCCAGGATAT CTGTTTGATG AATTGAATTG GTGCAATGGC AGTTTAAACAG	79
SM38	TCCAGGATAT CTGTTTGATG AATTGAATTG GTGTAATGGC AGTTTAAACAG	500
Consensus	GCAACACAAA ATACGGGACT GTATGTGGAT GCGATTATAA AAGTAATGTT	550
EST AWO17229 comp	-----	
EST A1067047 comp	-----	
EST N20756	GCAACACAAA ATACGGGACT GTATGTGGAT GCGATTATAA AAGTAATGTT	129
SM38	GCAACACAAA ATACGGGACT GTATGTGGAT GCGATTATAA AAGTAATGTT	550
Consensus	GTTTCATGCGT TCTGGCAAAG TGCTTCGGCT GAGTATGCCA GGAGAGCATC	600
EST AWO17229 comp	-----GGCT	24
EST A1067047 comp	-----	
EST N20756	GTTTCATGCGT TCTGGCAAAG TGCTTCGGCT GAGTATGCCA GGAGAGCATC	179
SM38	GTTTCATGCGT TCTGGCAAAG TGCTTCGGCT GAGTATGCCA GGAGAGCATC	600
Consensus	TGGTAACATC TTTGTGGTAC TGAATGGCTC GGTCAAAGCT CCATTTAATG	650
EST AWO17229 comp	-----	74
EST A1067047 comp	-----	
EST N20756	TGGTAACATC TTTGTGGTAC TGAATGGCTC GGTCAAAGCT CCATTTAATG	229
SM38	TGGTAACATC TTTGTGGTAC TGAATGGCTC GGTCAAAGCT CCATTTAATG	650
Consensus	AAAAATAAAC TTTTGGAAAA ATAGAACTAC CATTGGTTAA AACATCCTCG	700
EST AWO17229 comp	-----	123
EST A1067047 comp	-----	
EST N20756	AAAAATAAAC TTTTGGAAAA ATAGAACTAC CATTGGTTAA AACATCCTCG	279
SM38	AAAAATAAAC TTTTGGAAAA ATAGAACTAC CATTG-TTAA AACATCCTCG	699
Consensus	AGTACAACAA TTAACAGTGA AATTAGTTCA TAGTTTGGAA GATGTAAATA	750
EST AWO17229 comp	-----	173
EST A1067047 comp	-----	
EST N20756	A-----	280
SM38	AGTACAACAA TTAACAGTGA AATTAGTTCA TAGTTTGGAA GATGTAAATA	749
Consensus	ACCGACAAAC ATGTGAATCG TGGAGTCTGC AAGAACTTGC AAACAAGCTG	800
EST AWO17229 comp	-----	223
EST A1067047 comp	-----	
EST N20756	-----	280
SM38	ACCGACAAAC ATGTGAATCG TGGAGTCTGC AAGAACTTGC AAACAAGCTG	799
Consensus	AACTCTGTAC ATATTCCTTT TCGTTGCATT GACGATCCTT TAGAGTTCAG	850
EST AWO17229 comp	-----	273
EST A1067047 comp	-----	
EST N20756	-----	280
SM38	AACTCTGTAC ATATTCCTTT TCGTTGCATT GACGATCCTT TAGAGTTCAG	849
Consensus	ACATTATCAA TGCATTGAAA ATCCTGGCAA ACAACTATGT CAGTTTTTCAG	900
EST AWO17229 comp	-----	323
EST A1067047 comp	-----ATTGAAA	37
EST N20756	-----	280
SM38	ACATTATCAA TGCATTGAAA ATCCTGGCAA ACAACTATGT CAGTTTTTCAG	899

Figure 13C

Consensus	CTTCGACGAG GTCAAACGTC GAGACATTAC TCATACTTTT TCCGCTAGTC	950
EST AW017229 comp	CTTCGACGAG GTCAAACGTC GAGACATTAC TCATACTTTT TCCGCTAGTC	373
EST A1067047 comp	CTTCGACGAG GTCAAACGTC GAGACATTAC TCATACTTTT TCCGCTAGTC	87
EST N20756	-----	280
SM38	CTTCGACGAG GTCAAACGTC GAGACATTAC TCATACTTTT TCCGCTAGTC	949

Consensus	ATTTGTTTAA CTTTTTATAC TTCCATGAAT TGAAATAACT TTTCAGAACT	1000
EST AW017229 comp	ATTTGTTTAA CTTTTTATAC TTCCATGAAT TGAAATAACT TTTCAGAACT	423
EST A1067047 comp	ATTTGTTTAA CTTTTTATAC TTCCATGAAT TGAAATAACT TTTCAGAACT	137
EST N20756	-----	280
SM38	ATTTGTTTAA CTTTTTATAC TTCCATGAAT TGAAATAACT TTTCAGAACT	999

Consensus	AAACTTTGAA CAGAGAAAGA GAACAATGAT AATAAAGGAA TAGGMCATTA	1050
EST AW017229 comp	AAACTTTGAA CAGAGAAAGA GAACAATGAT AATAAAGGAA TAGGCCATTA	473
EST A1067047 comp	AAACTTTG--	145
EST N20756	-----	280
SM38	AAACTTTGAA CAGAGAAAGA GAACAATGAT AATAAAGGAA TAGGACATTA	1049

102407-97928660

## Figure 14

GGAAAGAACGTAGACATATATTGTTATATAGATTTGTTTCAGTTATTTTTTCACAATCTTTTAATTCAAATA 70  
E R T . T Y I V I . I C S V I F H N L L I Q I

ATGATGAACGTAATATTGTTTCTTACTTTATCAAATATTTTTGCTTTAACTCTGCACAACATCAAATAA 140  
M M N V I L F L T L S N I F V F N S A Q H Q I

ACTTACTTAGTGAAATAGTACAATCAGGATGTACTCAGTGGAAGGTTGAACATGGAGCTACTAATATAAG 210  
N L L S E I V Q S R C T Q W K V E H G A T N I S

TTGTAGTGAGATCTGGAATTCATTTGAAAGCATTTTACTTTCAACTCATACTAAATCAGCATGTGTTATG 280  
C S E I W N S F E S I L L S T H T K S A C V M

AAATCAGGGTTATTCGATGATTTTGTATCAATTGTTTGAATTGGAACAACAACAACAGCGACACC 350  
K S G L F D D F V Y Q L F E L E Q Q Q Q Q R H

ACACAATTCAAACGGAACAATACTTCCATTCTCAAGTGATGAACATCATTCGTGGAATGTGTAAACGTCT 420  
H T I Q T E Q Y F H S Q V M N I I R G M C K R L

TGGAGTATGTCGTTCTCTAGAACTACATTTCCAGGATATCTGTTTGATGAATTGAATTGGTGTAAATGGC 490  
G V C R S L E T T F P G Y L F D E L N W C N G

AGTTTAAACAGGCAACACAAAAATACGGGACTGTATGTGGATGCGATTATAAAAGTAATGTTGTTTCATGCGT 560  
S L T G N T K Y G T V C G C D Y K S N V V H A

TCTGGCAAAGTGCTTCGGCTGAGTATGCCAGGAGAGCATCTGGTAACATCTTTGTGGTACTGAATGGCTC 630  
F W Q S A S A E Y A R R A S G N I F V V L N G S

GGTCAAAGCTCCATTTAATGAAAATAAACTTTTGGAAAAATAGAACTACCATTGTAAAACATCCTCGA 700  
V K A P F N E N K T F G K I E L P L L K H P R

GTACAACAATTAACAGTGAAATTAGTTCATAGTTTGAAGATGTAAATAACCGACAAACATGTGAATCGT 770  
V Q Q L T V K L V H S L E D V N N R Q T C E S

GGAGTCTGCAAGAAGCTTGAACAAGCTGAAGTCTGTACATATTCCTTTTTCGTTGCATTGACGATCCTTT 840  
W S L Q E L A N K L N S V H I P F R C I D D P L

AGAGTTCAGACATTATCAATGCATTGAAAATCCTGGCAAACAACATATGTCAGTTTTTCAGCTTCGACGAGG 910  
E F R H Y O C I E N P G K Q L C Q F S A S T R

TCAAACGTCGAGACATTACTCATACTTTTTCCGCTAGTCAATTTGTTTAACTTTTTTATCTTCCATGAATT 980  
S N V E T L L I L F P L V I C L T F Y T S M N

GAAATAACTTTTCAGAACTAACTTTGAACAGAGAAAGAGAACAAATGATAATAAGGAATAGGACATTAA 1050  
N N F S E L N F E Q R K R T M I I K E . D I N

TGAAAAAAAAAAAAAAAAAAAAA 1073  
E K K K K K K

TCTCT" 9792660



[illegible]

Consensus	M.....L.....S.....I.....L.....RC.....	50
Aplysia cd38p	MSPVAIVACV CLAVTLTRIS PSEAIPTPE LQNVLGRCK DYEITRYLTI	50
SM38p	M--MNVILFL TLSNIFVFNS AQHQI---NL LSEIVQSROT QWKVEH---	41
Consensus	.....C...W..F.....K..C...G...DF.....	100
Aplysia cd38p	LPRVKSDCRA LWTNFFKAFS F---KAPCNL DLGSYKDFEQ RAQQTLPKNK	97
SM38p	-GATNISCSE IWNSEFESILL STHTKSACVM KSGLFDDFVY QLFELEQQQQ	90
Consensus	.....*.....LE.T.PGY.....L.WC..	150
Aplysia cd38p	VMFWSGVYDE --AHDF--- ADDGRKYI-- -TLEDTLPGY MLNSLWCGQ	138
SM38p	QRHHTIQTEQ YFHSQVMNII RGMCKRLGVC RSLETTTFPGY LFDELWVNG	140
Consensus	.....VC....D...FW..A S..YA..A.G.....GS.	200
Aplysia cd38p	RDKPGFNQK- VQPDFKDCPV QARESFWGTA SSSYAHSAEG DVTYMVDSN	187
SM38p	SLTGNTKYGT VC--GCDYKS NVVHAFWQSA SAEYARRASG NIFVVLNGS-	186
Consensus	.....*.....FGK.ELP.L.....V.....H.L.....C...SL	250
Aplysia cd38p	PKVPAYRPDS FFGKYELPNL TNK-MTKVKV IVLHQLGQKI I-ERQAGSL	235
SM38p	-VKAPFNENK TFGKIELPLL KHPRVQQLTV KLVSLEDVN NRQTCESWSL	236
Consensus	..L.....F.C...P.....C..NP....CQ.....	300
Aplysia cd38p	LDLEMVVAK KFGFDVENP KSVLFLCAD NPNAREQLA KRYYRIA---	282
SM38p	QELANKLSNV HIPFRCIDDP LEFRHYQIE NPGKQLCQFS ASTRSNVETL	286
Consensus	.....	317
Aplysia cd38p	-----	282
SM38p	LILFLVLICL TFYTSMN	303
Consensus	M.....L.....L.....Q.....	50
Human CD38	MANCEFSPVS GDKPCCRLSR RAQLCLGVSI LVLILVVVLA VVPRWRQW	50
SM38p	M-----MNVLFLTLS NIFVFNSAQ-	20
Consensus	.....E.V..RC.....C...W..F.....S.H.K.	100
Human CD38	SGPGTTKRFP ETVLARC VKY TEIHPMRHV DCQSVWDAFK GAFIS--KH	97
SM38p	---HQINLLS EIVQSROTQW -KVEHGATNI SCSEIWNSE SILLSTHTKS	66
Consensus	.C.....YQ.....S.....	150
Human CD38	PONITEED-- --YQPLMKL GTQVPCNKI L----LWSRI KDLAQFTQV	138
SM38p	ACVMKSGLFD DFVYQLFELE QQQQRHHTI QTEQYFHSQV MNII RGMCKR	116
Consensus	.....*.....LE.T..GYL.D.L.WC....T...Y...C....C....N.V	200
Human CD38	QRDMFTLEDL LLGYLADDLT WCGEFNTSKI NYQS-CPDWR KDC--SNNPV	185
SM38p	LGVCRSLETT FPGYLFDELN WCNGLTGT KYGTVCG--- --CDYKSNVV	161
Consensus	..FW...S...A.A.A....V.LNGS....F..N.TFG...*...L...V	250
Human CD38	SVFWKTVSRR FAEAACDVVH VMLNGSRSKI FDKNSTFGSV EVHNLQPEKV	235
SM38p	HAFWQSASAE YARRASGNIF VVLNGSVKAP FENKTFGKI ELPLLKHPRV	211
Consensus	Q.L.....H.....R..C.....EL...I.F.C.....	300
Human CD38	QTLEAWVHG GRE-DSRDLC QDPTIKELIS IISKRNIOFS CKNIYRPDKF	284
SM38p	QQLTVKLVHS LEDVNNRQTC EWSLQELAN KLSNVHIPER CIDDPLEFRH	261
Consensus	.QC..NP...C.....TS..	342
Human CD38	LQCVKNPDS SC-----TS EI	300
SM38p	YQCIENPGKQ LQFSASTRS NVETLLILFP LVICLTFYTS MN	303

**B.**

MMNVILFLTL	SNIFVFNSAQ	HOINLLSEIV	OSRCTOWKVE	HGATNISCSE	50
IWNSFESILL	STHTKSACVM	KSGLFDDFVY	QLFELEQQQQ	QRHHTIQTEQ	100
YFHSQVMNII	RGMCKRLGVC	RSLETTFPGY	LFDELNWCNG	SLTGNTKYGT	150
VCGCDYKSNV	VHAFWQSASA	EYARRASGNI	FVVLNGSVKA	PFNENKTFGK	200
IELPLLKHPR	VOQLTVKLVH	SLEDVNNROT	CESWSLOELA	NKLNSVHIPE	250
RCIDDPLEFR	HYOCIEENPGK	QLCOFSASTR	SNVETLLILF	PLVICLTFYT	300
SMN					303

Figure 16

ATGATGAAYG	TNATHYTNTT	YYTNACNYTN	WSNAAYATHT	TYGTNTTYAA	50
YWSNGCNCAR	CAYCARATHA	AYYTNYTNS	NGARATHGTN	CARWSNMGNT	100
GYACNCARTG	GAARGTNGAR	CAYGGNGCNA	CNAAYATHWS	NTGYWSNGAR	150
ATHTGGAAYW	SNTTYGARWS	NATHYTNYTN	WSNACNCAYA	CNAARWSNGC	200
NTGYGTNATG	AARWSNGGNY	TNTTYGAYGA	YTTYGTNTAY	CARYTNTTYG	250
ARYTNGARCA	RCARCRCAR	CARMGNCAYC	AYACNATHCA	RACNGARCAR	300
TAYTTYCAYW	SNCARGTNAT	GAAYATHATH	MGNGGNATGT	GYAARMGNYT	350
NGGNGTNTGY	MGNWSNYTNG	ARACNACNTT	YCCNGGNTAY	YTNTTYGAYG	400
ARYTNAAYTG	GTGYAAYGGN	WSNYTNACNG	GNAAYACNAA	RTAYGGNACN	450
GTNTGYGGNT	GYGAYTAYAA	RWSNAAYGTN	GTNCAYGCNT	TYTGCCARWS	500
NGCNWSNGCN	GARTAYGCNM	GNMGNGCNWS	NGGNAAYATH	TTYGTNGTNY	550
TNAAYGGNWS	NGTNAARGCN	CCNTTYAAYG	ARAAYAARAC	NTTYGGNAAR	600
ATHGARYTNC	CNYTNYTNAA	RCAYCCNMGN	GTNCARCARY	TNACNGTNAA	650
RYTNGTNCA	WSNYTNGARG	AYGTNAAYAA	YMGNCARACN	TGYGARWSNT	700
GGWSNYTNCA	RGARYTNGCN	AAYAARYTNA	AYWSNGTNCA	YATHCCNTTY	750
MGNTGYATHG	AYGAYCCNYT	NGARTTYMGN	CAYTAYCART	GYATHGARAA	800
YCCNGGNAAR	CARYTNTGYC	ARTTYWSNGC	NWSNACNMGN	WSNAAYGTNG	850
ARACNYTNYT	NATHYTNTTY	CCNYTNGTNA	THTGYYTAC	NTTYTAYACN	900
WSNATGAAY					909

Figure 17